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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,251	11/01/2001	Robert K. Naviaux	UCSD1140-1	9760

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EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	PAPER NUMBER
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/889,251	NAVIAUX, ROBERT K.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *67,70,73-81,84-91 and 95-110* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *67,70,73-81,84-91 and 96-109* is/are rejected.

7)☒ Claim(s) *95 and 110* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's Response filed February 2, 2007, which was timely filed and fully responsive, is acknowledged. Claims 67, 70, 73-81, 84-91 and 95-110 remain under consideration.

Applicant's arguments have been fully considered and are persuasive. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are newly applied. They constitute the complete set being applied to the instant application. In light of the new rejections being applied against the instant claims, the previous indication of finality is withdrawn and this Office Action is NON-FINAL.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 67, 70, 73-80, 81, 84-89, 91 and 96-108 are rejected under 35 U.S.C. 102(e) as being anticipated by Nagley et al., U.S. Patent 5,981,601.

Nagley teaches the administration of uridine, including functional derivatives and/or precursors thereof, to treat a mitochondrial disorders wherein at least one mutation in the mitochondria has occurred. Primarily, Nagley's teaching is drawn to the mitochondrial toxicity and physiologic effects that result from the administration of the of the reverse transcriptase inhibitor drug AZT. See claims 1, 5, 6, 10 and 18, column 18-20 and 24. AZT acts as a mitochondrial poison in that it causes cellular cytotoxicity, which is particularly manifest in muscle, causing myopathy. As a mitochondrial poison, AZT disrupts mitochondrial respiratory chain function resulting in a reduced capacity for generating ATP. Specifically, AZT affects the oxidation/phosphorylation system and the activity of complex I and IV of the mitochondrial respiratory chain. As required by instant claims 85, 86, 104 and 105, the administration of uridine may be accompanied by the administration of one or more co-factors or vitamins, such as coenzyme Q or an antioxidant as ascorbic acid. See Example 1, column 11. See column 5, lines 50-55, where Nagley's claimed redox compounds may include vitamins of the K series or ascorbic acid. See column 3, lines 50-60. Anti-oxidant scavengers include α-lipoic acid, as recited in instant claims 87 and 106. Further, other diseases associated with disruption of the mitochondrial respiratory chain function are also included in Nagley's teaching. See column 8, line 63,to column 9, line 10, where encephalomyopathy lactic acidosis is included among those mitochondrial pathologies contemplated. As required by instant claims 88, 89, 107 and 108, see column 7, lines 3-5, where the disclosed daily dosage range overlaps with those instantly claimed. The claimed recitation "about 2 gm/m^2 overlaps with Nagley's teaching of 2000 mg per day.

Functional limitations are recited in instant claims 74-79, 84, 96-100, 102 and 103. The claims are drawn to deficiencies of cardiolipin, of a pyrimidine synthetic pathway, of the uridine synthetic pathway, of the expression and/or activity of an enzyme in the pyrimidine synthetic pathway, such as dihydroorotate dehydrogenase or uridine monophosphate synthetase, and of lower than normal uridine levels. In the absence of a showing that these mechanisms of action are not present in a mitochondrial disorder, one skilled in the art would have considered such deficiencies to be inherent in the pathogenesis of the disease processes.

It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention").

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 67, 70, 73-81, 84-91 and 96-109 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nagley et al., U.S. Patent 5,981,601, in view of Page et al., Proc. National Academy of Sciences.

Nagley is applied as set forth *supra*. Nagley fails to teach the administration of uridine in a daily dosage of about 6.0 g/m^2. However, Page teaches the safe and effective administration of higher doses of uridine that approach about 6.0 g/m^2. See page 1603, column 2.

No claim is allowed.

Schorlemmer et al., International Journal of Immunotherapy (abstract), is cited to show further the state of the art with respect to inhibitors of DHODH, such as leflunomide and brequinar, in *de novo* pyrimidine biosynthesis.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached from 10:30 to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Ardin Marschel, can be reached 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

April 16, 2007

Phyllis Spivack

Phyllis Spivack

1614

PHYLLIS SPIVACK
PRIMARY EXAMINER